REMARKS

Claims 1-7, 26 and 37 have been amended, and claims 42-44 are new. Accordingly, the application as amended herein contains claims 1-16 and 24-44. Reconsideration of the application as amended is requested.

Claims 1, 26 and 37 have each been amended to remove the recitation limiting efavirenz to crystalline efavirenz, thereby broadening the scope of these claims. The "efavirenz is crystalline" feature has instead been captured in new claims 42-44, which depend from claims 1, 26 and 37 respectively. Support for new claims 42-44 can be found on page 2, line 1 and on page 7, lines 13 and 18-19. These passages refer to tablet compositions in which the loss of crystallinity of efavirenz is avoided or the crystallinity of efavirenz is maintained, and thus clearly show that efavirenz-containing compressed tablet compositions in which the efavirenz is crystalline form part of the invention.

Claims 1, 26 and 37 have also been amended to recite that the superdisintegrant concentration in the compressed efavirenz tablet is between about 1% to about 5% by weight. Support for these amendments can be found in the specification at lines 22 - 24 of page 3, in the table at the top of page 5, and in Example 8 on page 21. Page 3, lines 22-24 disclose that the superdisintegrant concentration can be varied between about 1% to about 20%. The table at the top of page 5 discloses a tablet composition in which the superdisintegrant concentration is 5% (i.e., 30 mg of croscarmellose sodium in a 600 mg tablet composition, excluding the coating). Similarly, Example 8 discloses a tablet composition in which the superdisintegrant concentration is 5%. This disclosure provides support for the 1% to 5% range cited in the claims. It is acknowledged that this range does not appear *in ipsis verbis* in the application, but such is not required. See, e.g., *In re Lukach*, 169 U.S.P.Q. 795, 796 (CCPA, 1971) and *In re Wertheim*, 191 U.S.P.Q. 90, 96 (CCPA, 1967) (stating "It is not necessary that the application describe the claim limitations exactly, but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that appellants invented processes including those limitations.") The claimed superdisintegrant concentration (i.e., between about 1% to about 5%) is nothing more than a portion of the range (i.e., about 1% to about 20%) described in the application as filed. In addition, compositions having a 5% superdisintegrant concentration are exemplified. In other words, the claimed superdisintegrant concentration range is reasonably conveyed to the person of ordinary skill in the art by the original application disclosure, and thus these claim amendments neither introduce new matter nor extend beyond the scope of the application as filed.

Claims 2-7 have been amended to replace "and" with "or" to indicate that the materials listed therein are to be employed alternatively not conjunctively. In addition, some materials recited in plural form have been changed to the singular to be consistent with the use of "or".

The phrase "such as lactose hydrous spray dried" modifying "lactose" in claim 6 has been removed.

The amendments to claims 2-7 do not narrow their scope.

None of the amendments introduces new matter into the application.

Marked up versions of the amended claims explicitly showing the added and deleted matter appear after the Remarks.

Priority

The priority claim for this application is domestic, not foreign as suggested on page 1 of the Detailed Action.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-16 and 24-41 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The gist of the rejection appears to be the Examiner's concern over the use of the conjunctive "and" in claims 1-7. The use of "comprising" with "and" in claim 1 is proper, in that claim 1 recites a tablet composition that includes each of the specified components following the term "comprising". Claims 2-7 depend from claim 1 and narrow its scope by limiting a particular component of the tablet composition to a specific list of materials. As discussed earlier, claims 2-7 have been amended to replace "and" with "or", thereby indicating that the materials listed in each of these claims represent alternatives.. With this amendment, any perceived confusion as to claim scope has been eliminated, and the claims are definite. Withdrawal of this rejection is requested.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-16 and 24-41 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner has asserted that the phrase "efavirenz is crystalline" lacks written description support in the application. The reference to crystalline efavirenz has been removed from claims 1-16 and 24-41 rendering this rejection moot as applied thereto. However, new claims 42-44 recite crystalline efavirenz. This rejection is traversed with respect to the new claims.

As noted earlier and repeated here, support for new claims 42-44 can be found on page 2, line 1 and on page 7, lines 13 and 18-19. These passages refer to tablet compositions in which the loss of crystallinity of efavirenz is avoided or the crystallinity of efavirenz is maintained, and thus clearly show that efavirenz-containing compressed tablet compositions in which the efavirenz is crystalline form part of the invention. It is acknowledged that the phrase "efavirenz is crystalline" does not appear *in ipsis verbis* in the application, but its appearance therein is not required (see *In re Lukach*, cited above). The written description requirement is satisfied if the

application reasonably conveys to the person of ordinary skill in the art that the applicant was, at the time the application was filed, in possession of the subject matter being claimed. The application clearly conveys that the applicants were in possession of tablet compositions containing crystalline efavirenz. Withdrawal of this rejection is accordingly requested.

Double Patenting

The claims have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of copending U.S. Serial Application No. 09/700,946. Application 09/700,946 has been abandoned by failure to file a response to the Office Action mailed May 30, 2002 (Paper No. 13) that complied with 37 C.F.R. § 1.113(c) or 37 C.F.R. § 1.114 and by failure to respond to the Advisory Action (Paper No. 15) mailed August 30, 2002. Withdrawal of the double patenting rejection is accordingly requested.

Rejection under 35 U.S.C. § 102

Claims 1-10, 24-28, 29-31 and 37-40 have been rejected under 35 U.S.C. § 102(e) as being anticipated by US 6,238,695 B1 ("Makooi"). This rejection is traversed with respect to the claims as amended herein and as applied to new claims 42-44.

Makooi discloses oral dosage forms that contain efavirenz and disintegrate rapidly (col. 2, lines 11-14). The oral dosage forms are capsules or compressed tablets comprising a therapeutically effective amount of efavirenz and a high level (greater than 10 wt.%) of disintegrant (col. 5, lines 8-13). Superdisintegrants selected from modified starches, croscarmellose sodium, carboxymethylcellulose calcium and crospovidone are disclosed to be the preferred disintegrants (col. 5, lines 14-17 and lines 54-56). More particularly, Makooi emphasizes that very high levels of superdisintegrants are employed in its formulations. In col. 3, lines 56-67, the reference teaches a process for manufacturing tablets or capsules using a "very high level" of a superdisintegrant in the wet granulation step, preferably about 20 to about 75 wt.% relative to the total dry weight of the materials used in the wet granulation step, and more preferably about 20 to about 55 wt.%. In col. 4, lines 56-61, the reference discloses that the wet granulation preferably contains 20 to 75 wt.% of sodium starch glycolate (a superdisintegrant), in contrast with the 1 to 10% that is used in typical wet granulations. Examples 1 and 2 in Makooi describe wet granulation capsule formulations containing 35.16 wt.% and 13.15 wt.% of superdisintegrant Na starch glycolate respectively, and Example 3 describes a wet granulation tablet formulation containing 20 wt.% Na starch glycolate. In summary, Makooi teaches efavirenz formulations in which the superdisintegrant concentration is greater than 10% and is preferably 20% or more.

The Makooi disclosure contains the statement in col. 3, lines 36-38 that superdisintegrants "generally are used at a low level in the solid dosage form, typically 1% to

10% by weight relative to the total weight of the dosage unit." Makooi is here making a comment on the state of the prior art. The nearly identical comment appears in Makooi's description of the prior art at col. 1, lines 54-57. The statement in col. 3 is not an embodiment of the invention being claimed by Makooi, and in fact contrasts sharply with Makooi's teaching that very high levels of superdisintegrant are required for solid dosage forms containing efavirenz. Makooi explicitly notes this contrast at col. 4, lines 56-61.

The claims as amended herein are distinctly different from the teachings of Makooi. The instant claims recite a compressed efavirenz tablet formulation in which the superdisintegrant concentration is between about 1% to about 5%, whereas Makooi teaches formulations that require more than 10% superdisintegrant. Withdrawal of the section 102(e) rejection is accordingly requested.

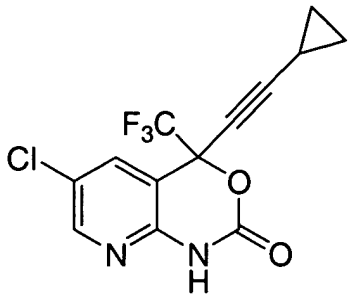
Rejection under 35 U.S.C. § 103

Claims 1-16 and 24-41 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Makooi in view of Remington: The Science and Practice of Pharmacy, 19th edition, pp. 1616-1620 ("Remington") and US 5,874,430 ("Christ et al."). This rejection is traversed with respect to the claims as amended herein and as applied to new claims 42-44.

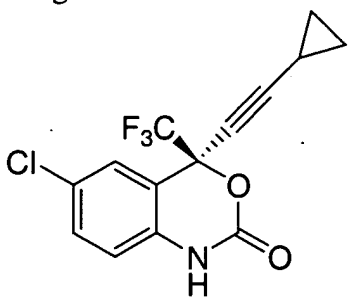
As set forth above in the remarks on the section 102(e) rejection, Makooi teaches efavirenz formulations containing greater than 10 wt.% superdisintegrant and preferably higher amounts thereof. In sharp contrast, the claimed invention is directed to formulations in which between about 1 wt.% to about 5 wt.% superdisintegrant is employed. Nothing in Makooi teaches or suggests efavirenz formulations containing 10 wt.% or less superdisintegrant. In fact, in emphasizing that very high levels of superdisintegrant are employed in its formulations, Makooi teaches away from the claimed invention. Makooi tells the person of ordinary skill in the art that, while superdisintegrants are typically employed at a low level (1-10 wt.%) in a solid dosage form (col. 1, lines 54-57), a low level of superdisintegrant is inappropriate for efavirenz formulations.

Remington provides a general description of tablet preparation and tablet ingredients. It does not disclose efavirenz and does not teach or suggest efavirenz-containing tablet compositions.

With respect to Christ et al., the Examiner has repeated an allegation made during the prosecution of the parent application; i.e., that the compound at col. 262, lines 45-50 of Christ et al. is efavirenz. This is NOT correct. The compound at col. 262, lines 45-47 is (+)-6-chloro-4-(cyclopropylethynyl)-4-trifluoromethyl-8-aza-1,4-dihydro-2H-3,1-benzoxazin-2-one which has the following structure:



Efavirenz is (-)-6-chloro-4-(cyclopropylethynyl)-4-trifluoromethyl-1,4-dihydro-2H-3,1-benzoxazin-2-one and has the following structure:



Accordingly, efavirenz is not the compound disclosed at col. 262, lines 45-47 of Christ et al. Efavirenz does not fall within the scope of the antiviral compounds claimed in Christ et al. The proviso located in col. 4, lines 9-15 excludes efavirenz from the compounds and compositions encompassed by the invention described in Christ et al. In fact, Christ et al. discloses efavirenz to be prior art (see col. 2, lines 42-58).

Christ et al. does teach compounds that are structurally similar to efavirenz and provides a general description of dosages and formulations for these compounds (cols. 249-250). However, the reference does not teach or suggest efavirenz-containing formulations, and, more particularly, does not teach or suggest efavirenz-containing compressed tablet compositions containing between about 1% to about 5% superdisintegrant.

The combination of Makooi, Remington, and Christ et al. does not teach or suggest the claimed invention. Assuming for the sake of argument that the skilled artisan were motivated to modify Makooi with the teachings of Remington and Christ et al., the skilled artisan would obtain formulations in which the concentration of superdisintegrant was more than 10%, in sharp contrast to the claimed compositions containing 1-5% superdisintegrant.

In view of the preceding remarks, reconsideration and withdrawal of the section 103(a) rejection is requested.

The application is believed to be in condition for allowance and passage to issue is requested. The Examiner is invited to telephone the undersigned should any minor matters need to be resolved before a Notice of Allowance can be mailed.

Respectfully submitted,

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Marked up versions of the amended claims are as follows, wherein an underline (added) denotes added material and a set of brackets ([deleted])denotes deleted material:

IN THE CLAIMS

1. (twice amended) A compressed tablet comprising: efavirenz, filler/disintegrant, superdisintegrant, binder, surfactant, diluent/compression aid, lubricant, and solvent, wherein efavirenz [is crystalline and] is from about 1 to about 75% by weight of the total composition of the compressed tablet, and the superdisintegrant has a concentration in the tablet between about 1% to about 5% by weight.

2. (amended) The compressed tablet, as recited in Claim 1, wherein the filler comprises: lactose, calcium carbonate, calcium sulfate, a compressible sugar, [sugars,] a dextrate, [dextrates,] dextrin, dextrose, calcium phosphate, kaolin, magnesium carbonate, magnesium oxide, maltodextrin mannitol, powdered cellulose, pregelatinized starch, or [and] sucrose.

3. (amended) The compressed tablet, as recited in Claim 2, wherein the disintegrant and superdisintegrant each comprise: alginic acid, carboxymethylcellulose calcium, carboxymethylcellulose sodium, colloidal silicon dioxide, croscarmellose sodium, crospovidone, guar gum, magnesium aluminum silicate, methylcellulose, microcrystalline cellulose, polyacrilin potassium, powdered cellulose, pregelatinized starch, sodium alginate or [and] starch.

4. (amended) The compressed tablet, as recited in Claim 3, wherein the binder comprises: acacia, alginic acid, carbomer, dextrin, ethylcellulose, gelatin, guar gum, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, liquid glucose, magnesium aluminum silicate, maltodextrin, methylcellulose, a polymethacrylate, [polymethacrylates,] povidone, pregelatinized starch, sodium alginate, starch, or [and] zein.

5. (amended) The compressed tablet, as recited in Claim 4, wherein the surfactant comprises: sodium lauryl sulfate, docusate sodium, benzalkonium chloride, benzethonium chloride, or [and] cetrimide.

6. (amended) The compressed tablet, as recited in Claim 5, wherein the filler/compression aid comprises: calcium carbonate, calcium sulfate, a compressible sugar, [sugars,] confectioner's sugar, a dextrate, [dextrates,] dextrin, dextrose, dibasic calcium phosphate dihydrate, glyceryl palmitostearate, hydrogenated vegetable oil (type I), kaolin, lactose, [such as lactose hydrous spray dried,] magnesium carbonate, magnesium oxide, maltodextrin, mannitol, a polymethacrylate, [polymethacrylates,] potassium chloride, powdered cellulose, pregelatinized starch, sodium chloride, sorbitol, starch, sucrose, sugar spheres, talc or [and] tribasic calcium phosphate.

7. (amended) The compressed tablet, as recited in Claim 6, wherein the lubricant comprises: calcium stearate, glyceryl monostearate, glyceryl palmitostearate, hydrogenated castor oil, hydrogenated vegetable oil, light mineral oil, magnesium stearate, mineral oil, polyethylene glycol, sodium benzoate, sodium lauryl sulfate, sodium stearyl fumarate, stearic acid, talc or [and] zinc stearate.

26. (amended) A compressed tablet comprising: efavirenz, filler/disintegrant, superdisintegrant, binder, surfactant, diluent/compression aid, lubricant, and solvent, wherein efavirenz [is crystalline and] is about 50% by weight of the total composition of the compressed tablet, and the superdisintegrant has a concentration in the tablet between about 1% to about 5% by weight.

37. (amended) A compressed tablet comprising: efavirenz, filler/disintegrant, superdisintegrant, binder, surfactant, diluent/compression aid, lubricant, and solvent; wherein efavirenz [is crystalline and] is from about 1 to about 75% by weight of the total composition of the compressed tablet, and the superdisintegrant has a concentration in the tablet between about 1% to about 5% by weight; and wherein the compressed tablet is prepared via wet granulation in which efavirenz, filler/disintegrant, superdisintegrant, binder, and surfactant are blended intragranularly, and filler/compression aid and lubricant are added extragranularly.